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Patent
030727.0037.CIP1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of:

Paul D. Van Poelje, et al.

Application No.: 09/900,364

Filed: July 5, 2001

Title: COMBINATION OF FBPASE INHIBITORS AND ANTIDIABETIC AGENTS USEFUL FOR THE TREATMENT OF DIABETES

Group Art Unit: 1614

Examiner: To be assigned

AMENDMENT AND RESPONSE TO NOTICE TO FILE CORRECTED APPLICATION PAPERS

Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

This communication is responsive to the Notice to File Corrected Application Papers mailed on September 7, 2001. Part 2 of that Notice is attached hereto.

As this response is being timely filed within the shortened two-month period for response indicated in the Notice, it is believed that no additional fee is due for this submission. If, however, any fee becomes payable, or any credit due, please charge or refund the same to Deposit Account No. 50-1273.

AMENDMENTS

Please amend the specification as follows:

In the Drawings

CERTIFICATE OF MAILING
(37 C.F.R. §1.8a)

I hereby certify that this paper (along with anything referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as First Class Mail in an envelope addressed to the Commissioner for Patents, Washington, D.C. 20231.

J. Gibbs
Name of Person Mailing Paper

10/11/01
Date of Deposit

Signature of Person Mailing Paper

Please add Drawings of Figures 1 and 2, on a separate sheet, as indicated in the accompanying Submission of Formal Drawings.

In the Specification

Please add a new section at page 23, line 14. The new section should read as follows:

--Brief Description of the Drawings

Figure 1 is a graphical representation of blood glucose level versus time associated with different treatments in Zucker Diabetic Fatty rats according to the invention; and

Figure 2 is a graphical representation of plasma lactate level versus time associated with different treatments in Zucker Diabetic Fatty rats according to the invention.--

In addition, please replace the paragraphs on page 316, line 15, to page 317, line 10, with the following paragraphs:

--Results: In pilot studies it was established that glyburide and Compound J were maximally efficacious in this model at doses of 100 and 300 mg/kg, respectively. In the current study, both glyburide and Compound J suppressed the rise in blood glucose levels induced by the oral glucose load, with compound J lowering blood glucose to below baseline levels (see Figure 1). Combination treatment was better than either monotherapy as indicated by the enhanced reduction in the area under the curve (AUC) of blood glucose during the initial 4 hours post drug administration:

Table 11:

Treatment	AUC glucose, mg/dL*h
Control	1463±99
Glyburide	1324±132
Compound J	1121±82
Combination	895±74

Combination treatment also attenuated the increase in blood lactate levels observed in the Compound J monotherapy group ($p = 0.01$ for 0 h timepoint, Figure 2).

This study indicates that combination treatment with an insulin secretagogue and an FBPase inhibitor provides significantly improved glycemic control over treatment with either agent alone. Improved glycemic control is likely to result in a reduced incidence of the complications associated with NIDDM. In addition, in this acute setting combination treatment attenuated a side effect associated with FBPase inhibitor therapy, blood lactate elevation. In a chronic setting this attenuation is more pronounced.--

REMARKS

In accordance with 37 C.F.R. §1.121, a marked up copy of the presently amended paragraphs of the specification is appended hereto. Deletions to the originally filed text are noted by bracketing. These amendments are being made merely to transfer Figures 1 and 2, originally included on page 317 of the specification, to a separate sheet of drawings. Accordingly, no new matter is added with these amendments.

Respectfully submitted,

BROBECK, PHLEGER & HARRISON LLP

Dated: 10-11-2001

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MARKED UP VERSION OF AMENDED PORTIONS OF THE SPECIFICATION

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